EXPERIMENT 2

Samples C, D and E

0.25 mg/ml of cyclosporin, 40 mg/ml of α-cyclodextrin and 7.79 mg/ml of sodium chloride (Sample C), or 0.10 mg/ml of cyclosporin, 20 mg/ml of α-cyclodextrin and 8.40 mg/ml of sodium chloride (Sample D) or 0.05 mg/ml of cyclosporin, 10 mg/ml of α-cyclodextrin, and 8.70 mg/ml of sodium chloride (Sample E) were dissolved in distilled water for injections. A trace of a 0.01N aqueous solution of sodium hydroxide was then added to each of these solutions to raise its pH to a value in the approximate region of 7, after which the solutions were filtered through a 0.22 μm filter. The cyclosporin concentrations, relative osmotic pressures (against physiological saline) and pH of the solutions were respectively as follows:

Sample C: 0.25 mg/ml, 1.04, 6.30;
Sample D: 0.09 mg/ml, 1.02, 6.86;
Sample E: 0.03 mg/ml, 1.02, 6.58.

Ocular Effects

0.05 ml of each of Samples A, C, D or E was applied in a single administration to the right eye of a male Japanese white rabbit. This administration was repeated a further 3 times (making 4 administrations in total) at intervals of 2 hours. 30 minutes after the last application, the cornea was excised as described in Experiment 1 and the cyclosporin levels in the corneal parenchyma were determined, also as in Experiment 1, averaging the results from 3 corneal samples. The results achieved were as follows:

A: 4900 ng/ml;
C: 4100 ng/ml;
D: 2200 ng/ml;
E: 1300 ng/ml.

The cyclosporin levels in the uvea were also determined and were found to be as follows:

A: 970 ng/ml;
C: 780 ng/ml;
D: 830 ng/ml;
E: 760 ng/ml.

This demonstrates that cyclosporin was successfully transferred into the ocular tissues. The level in the corneal parenchyma is important in relation to its use in keratoplasty, whilst that in the uvea is important in the treatment of Behcet's Syndrome.

We claim:

1. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a pharmaceutically effective amount of at least one cyclosporin in admixture with an amount of a functional derivative of α-cyclodextrin sufficient to solubilise the cyclosporin in water, wherein the α-cyclodextrin derivative is selected from the group consisting of α-cyclodextrin esters, α-cyclodextrin ethers, aminoalkylated derivatives of α-cyclodextrin, salts of α-cyclodextrin with a sulfur-containing acid, carboxyalkylated derivatives of α-cyclodextrin, addition compounds of α-cyclodextrin with a monosaccharide, addition compounds of α-cyclodextrin with a disaccharide, polymers comprising α-cyclodextrin in their main chain and polymers comprising α-cyclodextrin pendant on their main chain.

2. The composition of claim **1**, wherein the weight ratio of said cyclosporin to said α-cyclodextrin derivative is from 1:0.5 to 1:1000.

3. The composition of claim **1**, wherein the weight ratio of said cyclosporin to said α-cyclodextrin derivative is from 1:1 to 1:200.

4. The composition of claim **1**, wherein the α-cyclodextrin derivative is selected from the group consisting of acetylated α-cyclodextrin, methylated α-cyclodextrin, aminoethyl-α-cyclodextrin, α-cyclodextrin sulfate and maltosylated α-cyclodextrin.

5. The composition of claim **1**, wherein said cyclosporin is selected from the group consisting of cyclosporin A, cyclosporin B, cyclosporin D and cyclosporin G.

6. The composition of claim **1**, wherein said α-cyclodextrin derivative is a α-cyclodextrin ester in which some or all of the hydroxy groups in the glucose units are acylated and the acyl groups are derived from an acid selected from the group consisting of (a) a carboxylic acid, said carboxylic acid selected from the group consisting of acetic acid, propionic acid, butyric acid, valeric acid, isovaleric acid, pivalic acid, fumaric acid, succinic acid, citric acid, tartaric acid, oxalic acid and maleic acid; (b) a sulfonic acid, said sulfonic acid selected from the group consisting of methanesulfonic acid, trifluoromethane sulfonic acid, ethanesulfonic acid, benzenesulfonic acid and p-toluene sulfonic acid; and (c) an amino acid, said amino acid selected from the group consisting of glutamic acid and aspargic acid.

7. The composition of claim **1**, wherein said α-cyclodextrin derivative is an ether derivative wherein the ether moiety is an alkyl group having 1 to 4 carbon atoms.

8. The composition of claim **1**, wherein said α-cyclodextrin derivative is an aminoalkylated derivative of α-cyclodextrin wherein the alkyl group has 1 to 4 carbon atoms.

9. The composition of claim **8**, wherein the aminoalkylated derivative of α-cyclodextrin is selected from the group consisting of aminomethyl-α-cyclodextrin and aminoethyl-α-cyclodextrin.

10. The composition of claim **1**, wherein said α-cyclodextrin derivative is a carboxyalkylated derivative having an alkyl group with 1 to 4 carbon atoms.

11. The composition of claim **10**, wherein said carboxyalkylated derivative is selected from the group consisting of carboxymethyl-α-cyclodextrin, carboxyethyl-α-cyclodextrin and carboxypropyl-α-cyclodextrin.

12. The composition of claim **1**, wherein said α-cyclodextrin derivative is an addition compound of α-cyclodextrin comprising a monosaccharide or a disaccharide which is condensed with a hydroxy group of an α-cyclodextrin derived from maltose, glucose, fructose, galactose, sucrose or lactose.

13. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a pharmaceutically effective amount of at least one cyclosporin in admixture with an amount of α-cyclodextrin sufficient to solubilise the cyclosporin in water.

14. The composition of claim **13**, wherein the weight ratio of said cyclosporin to said α-cyclodextrin is from 1:0.5 to 1:1000.

15. The composition of claim **13**, wherein the weight ratio of said cyclosporin to said α-cyclodextrin is from 1:1 to 1:200.

16. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a pharmaceutically effective amount of at least one cyclosporin and α-cyclodextrin or a functional derivative thereof dissolved in water, the amount of α-cyclodextrin or said